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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/014,887	12/11/2001	Geoffrey W. Krissansen	093397-0401	2382

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EXAMINER	
YAO, LEI	
ART UNIT	PAPER NUMBER
1642	
MAIL DATE	DELIVERY MODE
12/22/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/014,887	KRISSANSEN ET AL.	
	Examiner	Art Unit	
	LEI YAO	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,10,11,13-15,18,19,21-23,26,27,29-31,34,35,37-39 and 56-58* is/are pending in the application.

4a) Of the above claim(s) *10,11,15,18,19,23,26,27,31,34,35 and 39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 13-14, 21-22, 29-30, 37-38, 56-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/21/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Request for Continued Examination

The request filed on 10/21/2008 for a Continued Examination (RCE) under 37 CFR 1.114 based on Application No. 10014887 is acceptable, and a RCE has been established. An action on the RCE follows.

Claims 5-9, 12, 16-17, 20, 24-25, 28, 32-33, 36, and 40-55 are cancelled.

Claims 56-58 are added.

Claims 1-4, 10-11, 13-15, 18-19, 21-23, 26-27, 29-31, 34-35, 37-39, 56-58 are pending.

Claims 10-11, 15, 18-19, 23, 26-27, 31, 34-35, 39 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention,

Claims 1-4, 13-14, 21-22, 29-30, 37-38, 56-58, drawn to a method of treating for a mammal or a patient with a cancer by administering DMXAA and a DNA encoding B7.1, are examined on the merits.

Information Disclosure Statement

The information disclosure statement (s) (IDS) submitted on 10/21/2008 are/is considered by the examiner and initialed copies/copy of the PTO-1449 are/is enclosed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-4, 13-14, 21-22, 29-30, 37-38, and 56-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Emtage et al., (J Immuno. Vol 160, page 2531-38, 1998) in view of Wilson et al., (Int. J. Radiation Oncology Biol. Phys., Vol. 42, page 905-908, 1998, provided 10/9/2007) or Lash et al., (Br. J Cancer. Vol 78, page 439-45, 1998, abstract).

The claims are drawn to methods of treating a patient with advanced or large tumor comprising administering DNA encoding B7.1 in conjunction with tumor restricted agent DMXAA (claims 1 and 2) or potentiate the activity of B7.1 comprising administering the DNA encoding B7.1 and then tumor restricted agent DMXXA (claims 3 and 4) to eradicate an advanced or large tumors present in a patient, wherein B7.1 is administered in expression viral based vector prior to the

tumor restricted agent DMXXA (claims 13, 20-21, 28-29, 37, 56-58), wherein the method further includes the administering of an addition tumor growth-restricting agent (claims 14, 22, 30, 38).

Emtage et al., teach a method of treating established large breast tumor with B7.1 expressed in adenoviral expression vector in combination of IL-2 expression vector. Emtage et al., teach that the B7.1 viral expression vector is intratumorally administrated and the combination therapy induces more tumor regression than single treatment (page 2535, col 2 and table I). Emtage et al., also teach that the virus expressing B7.1 is administering at a dose $5x10^8$ plaque-forming unit (page 2535, col 2). Emtage et al., suggest that the antitumor activity through immune system is enhanced by supplying both B7.1 and IL-2 (page 2537, col 1). Emtage et al., also suggest that additional antitumor agent (s), such as IL-4, IL-12, and/or B7.2 could be used for augment of the antitumor activity (page 2536, col 1).

Emtage et al., do not teach a method of treating a tumor with antitumor agent DMXAA (5, 6, dimethyl anthenone-4-acetic acid XAA) in conjunction with the vector expressing B7.1.

Wilson et al., teach that 5, 6-dimethyl anthenone-4-acetic acid (DMXAA) induces TNF production (page 905, col 1) and potentiates tumor therapy comprising radiation response compared to each treatment alone (entire reference, especially, page 906, col 2, page 907, tables). Wilson et al., teach the treatment commenced when tumors reach to 0.4-0.6g (page 96, col line 5-8 from bottom).

Lash et al., also teach a method of treating a cancer with 5, 6-dimethyl anthenone-4-acetic acid (DMXAA) combined with another anti-cancer agent, 5-hydroxytryptamine (5-HT). Lash et al., teach that the anticancer activity of the agent is strongly potentiated by DMXAA (abstract).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to substitute one agent for cancer treatment by another agent having the same anti tumor function with a expected result. One of ordinary skill in the art at the time the invention was made would have been motivated to apply the teaching of Wilson et al., or Lash et al., to the method of Emtage et al., in order to benefit for the treatment of advanced or large tumor because Wilson et al., or Lash et al., have already shown that the response of the large tumor treatment to the radiation or 5-HT is potentiated by DMXAA during the combination therapy. One of ordinary skill in the art at the time the invention was made would have been motivated with reasonable expectation of success to modify the method of Emtage by substituting the IL-2 vector with DMXAA because Wilson et al., and Lash et al., show that DMXAA induces other antitumor cytokine productions during the treatment suggesting the successful combination treatment of two anti-tumor agents resulting from an additive result. One of ordinary skill in the art at the time the invention was made would have been motivated with reasonable expectation of success to modify the treatment schedule and the method steps by administering B7.1 prior to the DMXAA and into one or more sites in the tumor in order to optimize and increase the efficacy of the treatment because Emtage et al., have suggested the B7.1

activating T cells, as such, one skilled in the art would have been motivated to give the B7.1 DNA prior to the other antitumor agent that functions immediately in order to let the B7.1 protein expression and activating the T cell first. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

Regarding the limitations of administering DNA at dose of 60-180 μg recited in the claims, the Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the dose used in the art does not meet the requirement of the claimed dose range produced by 5x 10^8 pfu virus at defined time. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Applicant's arguments with respect to the claims above unpatentable over the references of Futami et al., in view of Wilson et al., and Olsson et al have been considered but are moot in view of the new ground(s) of rejection above.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-6.00pm Monday-Thursday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Lei Yao, Ph.D./
Examiner, Art Unit 1642

/Larry R. Helms/
Acting SPE of Art Unit 1643